# EXHIBIT 51

# Convective Warming Therapy Does Not Increase the Risk of Wound Contamination in the Operating Room

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Although convective warming therapy is effective in preventing hypothermia in anesthetized patients, little is known concerning the potential risks of its use. Hence, this balanced cross-over study was designed to determine if the use of convective warming therapy increased the risk of wound contamination. For 4 h, eight healthy male volunteers (aged 20–25 yr) lay supine on an operating room table with their lower bodies and legs covered with a warming cover and sterile surgical drape. The convective warming therapy was administered for 2 h. The other 2 h served as the control. In each session, culture plates were placed directly on the subject's abdomen through an opening in the drape. Tympanic membrane and leg skin temperatures were significantly higher with active warming. No significant differences in the number of bacterial colonies were observed between the two study periods. It was concluded that convective warming therapy, when appropriately applied, does not increase the risk for airborne bacterial wound contamination in the operating room.

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Wound infection is an important postsurgical problem. A wound infection complicates the recovery from an operation, can prolong the hospital stay, and substantially increases the cost of care. It has been estimated that a postoperative wound infection can increase the patient's stay approximately 6–14 days (1,2). In one study, decreasing the postoperative infection rate from 4.2% to 1.6% saved that institution approximately $750,000 over a 5-yr period (3). Reported rates for wound infection can range from 1% to 5% for "clean" cases and up to 6% for all cases (4,5).

Following studies in which the settling of bacteria onto sedimentation plates in the operating room were observed, specific guidelines for the rate of air turnover in the operating room were made by the Centers for Disease Control (5). A turnover rate of 20 exchanges per hour is considered necessary to minimize this potential source of contamination (6). With the recent advent of using convective based warming and/or cooling devices with airflows up to 15 $m^3$/min in close proximity to surgical patients, the potential risk for airborne bacterial contamination warranted reassessment. The present study was undertaken to test the hypothesis that the use of such therapy would be unlikely to increase a patient's risk for wound contamination during surgery.

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## Methods

This study was approved by the University of Minnesota Human Subjects Committee and was performed in three different operating rooms at the University of Minnesota Hospital during a 3-wk period. Eight healthy male volunteers (aged 20–25 yr), free of any cutaneous or systemic disease, and not having taken any antibiotics within a month before the study, gave informed consent for participation. Each subject was instructed to lay supine and relatively motionless on an operating room table for two consecutive 2-h trials. Their lower body and legs were covered with an operating room convection warming cover (Augustine Medical Inc., Eden Prairie, MN) with the adhesive edge securely applied at the level of the umbilicus. A sterile surgical drape with a chest opening was placed over the subject from the feet to the neck. The subject's skin was not surgically prepared or disinfected in any way. All subjects wore briefs and a surgical mask throughout the study.

The subjects inserted their own tympanic temperature probe (Mon-a-Therm Inc., St. Louis, MO) into their right ears. The wires were then secured to the patients by adhesive tape to prevent accidental removal. Self-adhesive skin temperature probes (Mon-a-Therm Inc.) were applied to the mid-thigh and the abdomen below the sternum. Temperatures were re-




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**Table 1.** Airborne Bacteria Detected During 2-h Trial Periods With and Without the Use of Convective Warming Therapy: Five Different Bacterial Types Were Cultured

| Subject and culture type† | | Control (no therapy) | Convective warming therapy |
|---|---|---|---|
| 1 | SBA | α-Streptococcus: 2 colonies<br>Coagulase (–)-Staph: 1 colony | *Sterile |
| | Mac | Sterile | Sterile |
| | CNA | Coagulase (–)-Staph: 1 colony | Coagulase (–)-Staph: 1 colony |
| 2 | SBA | *Coagulase (–)-Staph: 2 colonies<br>Bacillus: 1 colony | Coagulase (–)-Staph: 3 colonies |
| | Mac | Sterile | Sterile |
| | CNA | Coagulase (–)-Staph: 1 colony | Sterile |
| 3 | SBA | Coagulase (–)-Staph: 3 colonies | *Coagulase (–)-Staph: 4 colonies<br>Micrococcus: 1 colony |
| | Mac | Sterile | Sterile |
| | CNA | Coagulase (–)-Staph: 2 colonies | Sterile |
| 4 | SBA | Coagulase (–)-Staph: 2 colonies<br>Corynebacteria: 2 colonies | *Coagulase (–)-Staph: 2 colonies<br>Micrococcus: 1 colony |
| | Mac | Sterile | Sterile |
| | CNA | Coagulase (–)-Staph: 2 colonies<br>Corynebacteria: 1 colony | Coagulase (–)-Staph: 1 colony |
| 5 | SBA | *Coagulase (–)-Staph: 15 colonies<br>Corynebacteria: 1 colony | Coagulase (–)-Staph: 2 colonies |
| | Mac | Sterile | Sterile |
| | CNA | Coagulase (–)-Staph: 15 colonies<br>Corynebacteria: 1 colony | Sterile |
| 6 | SBA | *Coagulase ( )-Staph: 2 colonies | Coagulase (–)-Staph: 1 colony<br>Corynebacteria: 1 colony |
| | Mac | Sterile | Sterile |
| | CNA | Sterile | Coagulase (–)-Staph: 1 colony |
| 7 | SBA | Coagulase (–)-Staph: 2 colonies | *Corynebacteria: 1 colony |
| | Mac | Sterile | Sterile |
| | CNA | Sterile | Coagulase (–)-Staph: 1 colony |
| 8 | SBA | *Coagulase (–)-Staph: 1 colony | Sterile |
| | MAC | Sterile | Sterile |
| | CNA | Sterile | Sterile |

SBA = sheep blood agar; Mac = MacConkey; CNA = colistin-nalidixic acid; Staph = staphylococcus.
* = first set of data for that individual.

corded at 15-min intervals, and arterial blood pressures and heart rates were recorded using a Colin BP8800 automated blood pressure monitor (Colin Electronics Co. Ltd.) at 30-min intervals throughout the study. Three different types of bacterial culture plates were fastened to each subject's abdomen with double-sided tape at the start of each trial period, generating six plates per subject. The plate types were: 1) sheep blood agar (a nonspecific medium; six or more bacteria types may be detected); 2) MacConkey agar (a primary isolation medium for recovery of aerobic and anaerobic Gram-negative bacteria); and 3) colistin-nalidixic acid agar (inhibitory to Gram-positive organisms; six or more bacteria types may be detected). Subjects were randomly divided into two groups. One had the convective cover in place, but not inflated for the first 2-h period. The blowers (Bair Hugger Model 500, Augustine Medical, Inc.) were operational on the medium setting for the latter 2-h period. The other group had their trial periods reversed: i.e., the blowers were on initially. In this design, each subject served as his own control. A blower setting of medium corresponds to an airflow of 10.7 $m^3$/min at a temperature of 38 ± 3°C. At the end of the study period, the plates were cultured at 35°C for 48 h and read for the presence and type of bacteria.

Statistical significance of the temperature, heart rate, and blood pressure data was determined using Student's *t*-test, whereas the bacterial culture data were analyzed by a two-way analysis of variance. A $P$ value $< 0.05$ was considered significant.

## Results

No significant difference in the total number of bacterial colonies isolated on culture plates was observed

**Table 2.** Arterial Blood Pressure, Heart Rate, and Temperature Data at Selected Time Points for the Subjects in Each Study Group

| Control-therapy subjects 2, 5, 6, 8 | Time zero | 1 h of control | End of control | 1 h of warming | End of warming |
|---|---|---|---|---|---|
| Mean BP (mm Hg) | 98 ± 6.2 | 96 ± 3.3 | 95 ± 6.4 | 93 ± 3.1 | 98 ± 2.6 |
| HR (beats/min) | 72 ± 8.6 | 66 ± 7.5 | 66 ± 8.3 | 63 ± 6.7 | 70 ± 11.3 |
| Tympanic temp (°C) | 37.3 ± 0.4 | 36.7 ± 0.2 | 36.7 ± 0.3 | 36.8 ± 0.3 | 36.8 ± 0.2 |
| Thigh temp (°C) | 33.5 ± 1.0 | 35.2 ± 1.4 | 35.1 ± 1.4 | 37.1 ± 0.6 | 37.1 ± 0.4 |
| Abdominal temp (°C) | 33.7 ± 1.4 | 33.2 ± 1.2 | 32.2 ± 1.7 | 32.1 ± 1.9 | 32.9 ± 1.1 |
| **Therapy-control subjects 1, 3, 4, 7** | **Time zero** | **1 h of warming** | **End of warming** | **1 h of control** | **End of control** |
| Mean BP (mm Hg) | 99 ± 5.0 | 94 ± 7.3 | 93 ± 7.8 | 95 ± 7.5 | 94 ± 7.7 |
| HR (beats/min) | 77 ± 7.0 | 70 ± 7.1 | 69 ± 10.4 | 64 ± 5.1 | 71 ± 1.5 |
| Tympanic temp (°C) | 36.9 ± 0.2 | 36.8 ± 0.2 | 36.7 ± 0.2 | 36.5 ± 0.3 | 36.5 ± 0.3 |
| Thigh temp (°C) | 34.5 ± 1.3 | 33.0 ± 1.3 | 37.0 ± 0.2 | 32.1 ± 0.6 | 35.3 ± 0.3 |
| Abdominal temp (°C) | 34.0 ± 0.7 | 36.9 ± 0.2 | 33.1 ± 0.8 | 35.2 ± 0.3 | 32.1 ± 0.8 |

BP = blood pressure; HR = heart rate; temp = temperature.

between the two study periods. Five types of bacteria were isolated from the control plates: coagulase (–)-staphylococcus, corynebacteria, micrococcus, α-streptococcus, and bacillus. Only the first three types were isolated from the study plates (Table 1). The number of colonies of coagulase (–)-staphylococcus was significantly different between the groups, the control group having more colonies than the study group ($P < 0.05$).

There was no difference in arterial blood pressure or heart rate between the two trial periods (with and without active warming) or between the two groups (i.e., warming either initially or following a control period). In each group, there was a tendency for the heart rate to increase toward the end of each period, possibly in anticipation of completion (Table 2). Similarly, the temperature of the exposed skin of the abdomen in the region of culture dish placement was not significantly different between groups (Table 2). The averaged tympanic membrane temperatures for the subjects in the control therapy group decreased initially then rose slightly during warming, whereas temperatures of the other subjects decreased slightly during both warming and control (Table 2). Pooled tympanic membrane temperature data from both groups are presented in Figure 1. As expected, thigh skin temperatures were significantly higher during warming ($P < 0.05$). No subject reported feeling uncomfortably cold or began to shiver during either part of the study.

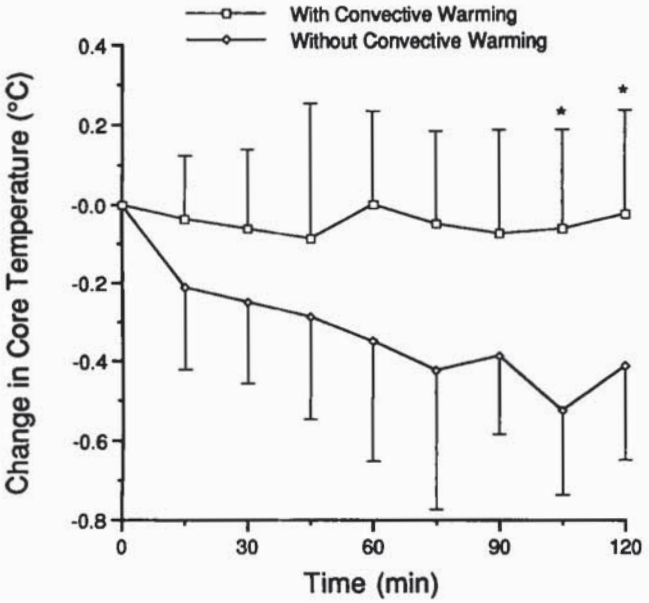


**Figure 1.** The effects of convective warming on core temperature (tympanic). The temperature data were normalized (per individual), and data for all subjects were pooled. With active warming, the core temperature was stable, whereas without warming a significant decrease was noted by the end of the control periods. * Significant difference ($P < 0.05$).

## Discussion

With the potential for convective-based warming devices to become commonplace in the operating room, it is important to assess their potential contribution to airborne bacterial contamination. The use of these devices raises some concern because they can contribute high air flows in close proximity to the patient. The relation between air movement and aerosolization of bacteria has been studied for years. The most significant sources of airborne bacteria are the patient (7), the surgical team (8), and even personnel in the corridors surrounding the operating room suite (6). Methods studied to combat this threat include "ultra-clean" laminar air flow rooms (8) and clothing with small pore size to limit the shedding of bacteria-laden skin particles (9).

This study was designed to evaluate the settling of bacteria at a simulated surgical site, an obvious prerequisite for the development of a wound infection via airborne bacteria. This design could be considered as simulating a "worst case scenario" because the subject's skin was not disinfected in any way. In addition, the awake subjects were free to move their upper extremities and talk, thus possibly contributing to the number of airborne particles. We hypothesize that if the subjects would have received a full antibacterial treatment prior to the study, the number of colonies cultured on the plates might have been fewer. Although there were no surgical personnel in the operating room suite, the investigators (who were not scrubbed) were frequently moving in and out of the room.

The bacteria most commonly detected in the present study was coagulase (–)-staphylococcus, an organism commonly associated with aerosolized contamination and a leading cause of postoperative wound infections (7). Of surprise was the absence of *Staphylococcus aureas*, which is among the most common pathogens isolated in studies of serious wound contamination and infection (8). A possible explanation for this difference between studies could be in the product design: the floor mounted blower used in the present study is designed with a 0.2-μm filter at the air intake, this size being much smaller than the average size of bacteria-carrying particles (20 μm) (9). In addition, the adhesive strip on the warming cover is applied at the waist, serving to direct the flow of air away from the surgical site and the surgical personnel.

As predicted, the decrease in core temperature observed in these unanesthetized subjects was much less than that commonly seen in anesthetized patients placed in a similar operating room environment (i.e., 1°C) (10,11). Anesthetized patients are considered to have disruption within their thermoregulatory mechanisms as well as anesthetic-induced cutaneous vasodilatation (12).

In conclusion, convective warming therapy, when properly applied to direct the flow of air away from the surgical site, does not increase the risk for wound contamination in the operating room.

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